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Case Report

Coexistence of two sclerotic bone diseases manifesting as spondyloarthropathy: Double trouble

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ABSTRACT

Hypoparathyroidism and fluorosis are two distinct sclerotic bone diseases. Both have high BMD but they behave differently. Fluorosis causes secondary hyperparathyroidism and has been reported to cause renal dysfunction. Here we discuss a case that coincidentally had both the disorders and their interaction.

1. Introduction

Osteosclerosis is characterized by high bone mineral density (BMD) often found incidentally in disorders like hypoparathyroidism, renal osteodystrophy, fluorosis and osteopetrosis (Whyte, 1997). Amongst these sclerotic bone disorders fluorosis and hypoparathyroidism are common and having many overlapping clinical and radiological features. Both have generalized osteosclerosis with high BMD. However, fluorosis causes secondary hyperparathyroidism and has been implicated in renal dysfunction (Harinarayan et al., 2006). Idiopathic hypoparathyroidism is an uncommon disorder which can present at any age and can be associated with celiac disease and other autoimmune disorders (Bhadada et al., 2011). Co-occurrence of both disorders poses a diagnostic dilemma and they interact with each other and alter clinical manifestation and its management. We report one such patient who has both and followed up for a period of 5 years.

2. Case report

A 54-year-male presented with low backache, episodes of carpopedal spasm for four years and fragility fracture of left sub-trochanteric femur. He had pigmentation of teeth. There was no history of renal stone disease, chronic diarrhea, mucocutaneous candidiasis, connective tissue disorder, neck surgery, irradiation, seizure or prior exposure to bisphosphonates.

On examination, he had a BMI of 26.03 kg/m^2. Dental examination showed hypoplastic areas with brownish discoloration, mottling without pitting suggesting a moderate grade dental fluorosis. There was no Albright's hereditary osteodystrophy (AHO) phenotype, vitiligo or goiter. He had positive Chvostek's and Trousseau signs. He also had proximal muscle weakness and restriction of movements at spine and both hip joints.

Blood investigations were consistent with hypo-parathyroidism (Table 1). Celiac serology and autoimmune workup were negative. 24 hour urinary fluoride 1 mg/L (normal: <1.5 mg/L) and ground water fluoride level 0.52 mg/L (normal: <0.5–1 mg/L).

X-ray of the forearm revealed interosseous membrane calcification (Fig. 1) and X ray of the hip showed obturator membrane calcification suggestive of skeletal fluorosis (Fig. 2). X-ray of the lumbar spine showed calcification of posterior longitudinal and interspinous ligaments (Fig. 3).

Bone density by DXA revealed a T-score of +7.45 SD at the spine, +3.06 SD at the left femur neck and +0.67 SD at distal radius (Table 2). Ultrasound examination showed normal kidney size and echotexture.

A diagnosis of hypoparathyroidism with skeletal fluorosis was made and was managed with oral calcium and calcitriol with which his carpopedal spasm subsided and backache improved. He had nonunion of fracture neck of femur and underwent open reduction and internal fixation. Over the next 5 years his iPTH (1.07 pg/mL) remained very low but the BMD progressively increased. His serum creatinine and GFR remained stable.

3. Discussion

We have discussed the coexistence of two sclerotic bone disorders and their interaction to modify clinical, radiological and biochemical parameters in a single patient.

Whyte and others described high BMD as a Z-score ≥+2.5 (Whyte, 2005; Gregson et al., 2012). Osteosclerosis or high BMD

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Table 1
Baseline parameters.

Parameters	Value	Reference range
Calcium-corrected for albumin	5.1 mg/dL	8.6–10.2 mg/dL
Phosphorus	5.3 mg/dL	2.5–4.5 mg/dL
Alkaline phosphatase	146 U/L	40–129 U/L
Urea	50 mg/dL	10–50 mg/dL
Creatinine	1.6 mg/dL	0.5–1.3 mg/dL
e GFR	41 mL/min	>90 mL/min
iPTH	<3 pg/mL	15–65 pg/mL
25(OH) vitamin D	19.8 ng/mL	Normal: 11.1–42.9 ng/mL
24 hour urine calcium	12.5 mg/24 h	600–2000 mg/24 h
24 hour urine phosphorus	450 mg/24 h	400–1300 mg/24 h
24 hour urine protein	600 mg/24 h	Normal: 50–150 mg/24 h
Tmp/GFR	5.8 mg/dL	2.4 to 4.2 mg/dL

states can be either diffuse or localized. Diffuse sclerotic disorders include fluorosis, renal osteodystrophy, hepatitis C-associated osteosclerosis, osteopetrosis, pycnodysostosis and hypoparathyroidism (Whyte, 1997).

Our patient had hypocalcemia, hyperphosphatemia, very low iPTH with early onset cataract and no evidence of autoimmune polyendocrinopathy. There was no similar family history and he remained asymptomatic till 48 years of age and hence a diagnosis of sporadic idiopathic hypoparathyroidism was made. Hypoparathyroidism is a chronic low bone turn over state with reduced bone remodeling and increased BMD in cortical and cancellous bones (Rubin et al., 2008). Laway et al. (2006) showed that the mean BMD values in patients with idiopathic hypoparathyroidism were significantly higher at lumbar spine and hip (16 · 3% and 9 · 6%) compared to controls. He also noticed that BMD increased with duration of disease. Our patient also had a rising trend in BMD over the next 5 years.

Apart from hypoparathyroidism our patient also had dental fluorosis, interosseous and obturator membrane calcification. Along with these

Fig. 2. X-ray pelvis AP view showing generalized increased sclerosis, obturator membrane calcification (arrow) and left sub-trochanteric fracture with internal fixation.

features coexistence of such a high value of BMD also points towards simultaneous presence of skeletal fluorosis. Skeletal fluorosis is associated with increased bone mass, bone formation and resorption. However, the overall turnover is decreased with increased cortical thickness and porosity. The lamellar bone is replaced by woven bone (Farlay et al., 2010a). Tamer et al. (2007) found fluorosis as the cause in one third of the patients who had high BMD. The highest Z-score reported so far in literature with fluorosis is +14 at the lumbar spine, +6.6 at the femur, and +0.06 at the radius Kurland et al., 2007. Our patient's Z-score was +8.39 at the lumbar spine, +4.35 at the femur and +0.85 at the radius further favors the co-occurrence of fluorosis with hypoparathyroidism (Table 2).

Patients with hypoparathyroidism are at greater risk of non-pathological fracture of small bones (24% incidence by Rubin et al.,

Fig. 1. X-ray forearm showing interosseous membrane calcification.

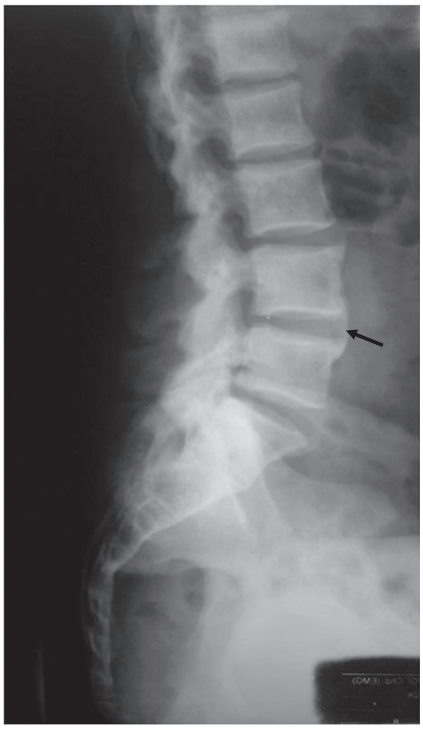

Fig. 3. X-ray lumbosacral spine showing increased sclerosis with calcified interspinous ligaments.

2008). Although bone is brittle in fluorosis, (Farlay et al., 2010b) fracture is otherwise uncommon (Teotia et al., 2004).

Both the disorders can have varying dental involvement, which is helpful in dating the onset of disease. Dental involvement is common in patients with hypoparathyroidism (Jensen et al., 1981 Feb). Our patient had a classical manifestation of dental fluorosis which suggests that fluorosis preceded hypoparathyroidism. Both fluorosis and idiopathic hypoparathyroidism can present as spondyloarthropathy. Radiological features may include the presence of syndesmophytes at thoraco-lumbar spine, mild sacroiliitis, and calcification at the acetabular margin of hip with preserved bone density (Ibn Yacoub et al., 2011; Goswami et al., 2008).

Our patient had stable renal dysfunction without any predisposing factors like hypertension, diabetes and recurrent urinary tract infection. Autopsy studies in patients with fluorosis showed chronic interstitial nephritis with tubular damage and secondary glomerular loss. Recently, the entity of fluorotoxic metabolic bone disease (FMBD) has been described in which concurrent renal calcium and phosphorus loss secondary to tubular damage, normal PTH and normal parathyroid gland has been observed (Harinarayan et al., 2006). Hypoparathyroidism is characterized by hypocalcemia which is an important predisposing factor for fluorosis.

To the best of our knowledge this is the first case in which co occurrence of these two disorders has been documented. This case gives us an opportunity to study how both of these disorders in the presence of renal dysfunction interact with each other. The coexistence of fluorosis and hypoparathyroidism is responsible for the higher BMD in our case and is likely that fluorosis predates idiopathic hypoparathyroidism in its onset. His BMD increased on follow-up, despite migrating to a non-fluorotic area and this can be attributable to absence of PTH and calcium supplementation. Both the disorders predisposed this patient to pathological fracture which is otherwise uncommon in either of the two diseases. Secondary hyperparathyroidism of fluorosis was masked by idiopathic hypoparathyroidism, hypercalciuria and phosphaturia in fluorosis is again blocked by hypoparathyroidism.

In conclusion, hypoparathyroidism and fluorosis have common clinical and radiological features. Coexistence of these leads to very high BMD and predisposes for pathological fracture and renal dysfunction. Timely diagnosis and treatment can reduce severity of symptoms.

Table 2
BMD of the patient.

	T-score			Z-score		
	Lumber spine	Left neck of femur	Distal radius	Lumber spine	Left neck of femur	Distal radius
2008	+7.45	+3.06	+0.67	+8.39	+4.35	+0.85
2011	+8.48	+3.97	+0.76	+9.24	+5.37	+0.92

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